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New Ways to Design Safer and More Effective Topical (Transdermal) Drug Delivery Announced in the Proceedings of the National Academy of Sciences

Could Injections Someday Be a Thing of the Past?

anta Barbara , Calif. ? March 14, 2005 ? In a paper published in the Proceedings of the National Academy of Scie nces, a group of researchers led by Samir Mitragotri , a professor of chemical engineering at the University of California, Santa Barbara, reports the identification of fundamental mechanisms that may facilitate the design of safer and more efficacious topical drug delivery systems.

Certain molecules, called chemical penetration enhancers (CPEs) help drugs absorb through the skin. After analyzing more than 100 different CPEs to better understand how they manage to increase skin permeability, the researchers engineered more than 300 new CPEs. The design of the new CPEs was based on the researchers? understanding of the molecular forces that are associated with CPE safety and potency. They then sc reened the new CPEs, first using computer technology and then testing the most promising ones in the laboratory environment. The molecules identified broaden the number of CPEs that can be used in the design of transdermal, cosmetic and pharmaceutical products.

?The methods used in this research not only increase our ability to create effective new CPEs, but they also will ex pand our ability to evaluate potential new CPEs for safety and efficacy,? said Mitragotri. ?By enhancing our abil ity to deliver drugs topically, we will be able to reduce the number of drugs that must be given by injection.?

The skin is composed of several layers. The top layer, Stratum Corneum (SC) is made of dead cells that contain proteins and lipid molecules which are arranged in bi-layers. The SC is a significant barrier to the absorption of drug molecules across the skin. CPEs help drug molecules penetrate into the skin by changing the structure of the SC.

Different CPEs penetrate the skin in unique ways. For example, some make microscopic holes in the SC by removing lipids. Others insert themselves in already-crowded lipid bi-layers to disorganize them. Some can also break open the dead cells in the SC and interact with the protein in those cells. CPEs that cause skin irritation are typically associated with the unfolding of proteins in skin cells.

By studying the molecular properties of a CPE, its propensity to penetrate or irritate the skin can be predicted. Simply put, the researchers draw a CPE?s structure on a computer, input its molecular properties, and then co mpute its penetrability or effectiveness and its potential to irritate the skin.

Such computer-aided modeling facilitates the analysis of millions of molecules, allowing researchers to then submit the most promising candidates to further in-vivo laboratory analysis.

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